REMARKS/ARGUMENTS

Status of the claims

Claims 53, 58-64, 70, 71, 74, 78- 88, and 93 to 100 were previously pending and presented for examination. Claims 53 and 78 are presently amended. Claims 59 to 64, 70, 71, 74,83 to 88, and 93 to 97 are canceled without prejudice. After entry of these amendments, claims 54, 58, 78 to 82, 99 and 100 will be pending.

Support for the amendments to the claims

Claims 53 and 78 were amended to set forth the portion of the PSCA protein of SEQ ID NO:2 comprising amino acid residues 2 through 50 as described in SEQ ID NO:2. This subject matter finds support *inter alia* in the specification as filed at page 23, the last two full paragraphs and also in claim 58. Accordingly, the Applicants believe the amendments to the claims add no new matter and respectfully request their entry.

Response to the rejection of claims 53, 58-64, 70, 71, 74, 78-88, 93-97, 99 and 100 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for the reasons previously set forth in the Office Action of December 28,2007, section 5, pages 2-11.

As previously noted by the Examiner and Applicants, whether undue experimentation is required to practice an invention is typically determined by evaluating: (i) the relative skill of those in the art; (ii) the nature of the invention; (iii) the breadth of the claims; (iv) the amount of guidance presented; (v) the presence of working examples; (vi) the state of the art; (vii) the predictability of the art; and (viii) the quantity of experimentation necessary. *Ex parte Forman*, 230 U.S.P.Q. 546 (PTO Bd. Pat. App. & Inter. 1986), *In re Wands*, 858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). The Applicants next remarks focus on those factors or concerns which were of a particular raised in the Office Action.

The principal concern of the Action was the enablement of the peptide fragment subject matter of the claims. The Applicants note that the use of whole protein antigens or large fragments thereof encoding antigen(s) allows host HLA molecules to select the appropriate

peptide epitope for presentation as a peptide-MHC complex on the cell surface. This approach does not require analysis of MHC molecules.

Accordingly, without acquiescing on the merits and in the spirit of expediting prosecution, the Applicants have amended the base claim to set forth fragments of the PSCA protein of SEQ ID NO:2 comprising amino acid residues 2 through 50 as described in SEQ ID NO:2. Accordingly, the PSCA subject matter of the base claims requires a portion of the PSCA protein which has particularly been shown to be a source of several suitable peptide fragments which have now been shown in the art, as next discussed, to be effective in generating an immune response.

In the paragraph bridging pages 10 and 11 of the Action, for instance, the Examiner acknowledged that the teachings of Thomas-Kaskel et al. were enabling for the PSCA 14-22 peptide-loaded dendritic cells. The PSCA protein and fragments of the claims embrace the Thomas-Kaskel epitope.

As noted previously, the Matsueda et al. reference reported that PSCA peptides (i.e., PSCA 7-15 and PSCA 21-30) were most active (see, Matsueda et al., Cancer Immunol. Immunother. 53:479-489 (2004)) in their vaccine trials in cancer patients. Matsueda et al., recognizably with expertise in the pertinent field, conducted their experiments, as evidenced by their Abstract, with an eye to the clinical significance of their findings. They specifically concluded that their two PSCA peptides should be considered for use in clinical trials of immunotherapy of prostate cancer.

With regard to the Zhang et al. reference, the Examiner was concerned that the PSCA vector (encoding the full protein) alone group did not appear to benefit from their DNA vaccines. However, it is noted that Zhang et al. also observed in the second sentence of their Abstract that DNA vaccines typically produce a less intense immune response which limits their clinical effectiveness. Hence, the need to use an adjuvant, such as HSP, given the mode of vaccination is not surprising and does not undercut the utility of the use of the full PSCA protein or its ability to be suitably processed *in vivo* to generate the immune response. The animals Zhang et al. treated with both the PSCA plasmid and the separate HSP plasmid did benefit from

the vaccinations in terms of both tumor size and survival. Thus, the Zhang et al. reference illustrates the ability of a DNA vaccination with the full PSCA protein to generate beneficial immune reactivity. In their research, Zhang et al. predicted and confirmed that human PSCA 28-36 was a H-2Db-restricted epitope which is recognized by MHC I molecules in treated animals and can induce peptide specific CD8+ immune responses in C56BL/6 mice (see, for instance, the third from the last paragraph of the reference). Thus, the reference pertains in particular to an epitope within the PSCA sequence set forth in the base claims.

Still more recently, Ahmad S, et al. have reported (*see*, Molecular Therapy (2009), enclosed) their isolation of the PSCA gene from the transgenic adenocarcinoma mouse prostate cell line (TRAMPC1) and construction of a vaccine plasmid. This plasmid PSCA (pmPSCA) was delivered by intramuscular electroporation (EP) and induced effective antitumor immune responses against subcutaneous TRAMPC1 tumors in male C57 BL/6 mice. The pmPSCA vaccination inhibited tumor growth, resulting in cure or prolongation in survival. Similarly, the vaccine inhibited metastases in PSCA expressing B16 F10 tumors. There was activation of Th-1 type immunity against PSCA, indicating the breaking of tolerance to a self-antigen. This immunity was tumor specific and was transferable by adoptive transfer of splenocytes. The mice remained healthy and there was no evidence of collateral autoimmune responses in normal tissues. They concluded that EP-assisted delivery of the pmPSCA evoked strong specific responses and could, in neoadjuvant or adjuvant settings, provide a safe and effective immune control of prostate cancer, given that there is significant homology between human and mouse PSCA.

As the PSCA fragment subject matter of the instant claims possess one or more suitable epitopes, the Applicants submit that persons of ordinary skill in the art can practice the claimed invention without undue experimentation. Accordingly, the Applicants respectfully request reconsideration and withdrawal of the rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

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